```
  result in loss of user privileges and other penalties.

  * * * * * * * * * * * * * * STN  Columbus  * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 10:30:26 ON 15 JUN 2004

=> file .meeting
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that are available.  If you have requested multiple files, you can
specify a corrected file name or you can enter "IGNORE" to continue
accessing the remaining file names entered.
ENTER A FILE NAME OR (IGNORE):ignore
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                         ENTRY    SESSION
FULL ESTIMATED COST                                       0.21       0.21

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=> EGFRvIII
L1             0 FILE AGRICOLA
L2            65 FILE BIOTECHNO
L3             0 FILE CONFSCI
L4             0 FILE HEALSAFE
L5             0 FILE IMSDRUGCONF
L6            41 FILE LIFESCI
L7             0 FILE MEDICONF
L8            51 FILE PASCAL

TOTAL FOR ALL FILES
L9           157 EGFRVIII

=> l9 same ELISA same antibody
MISSING OPERATOR L9 SAME
The search profile that was entered contains terms or
nested terms that are not separated by a logical operator.

=> EGFRvIII same ELISA same antibody
```

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L10             0 FILE AGRICOLA
L11             0 FILE BIOTECHNO
L12             0 FILE CONFSCI
L13             0 FILE HEALSAFE
L14             0 FILE IMSDRUGCONF
L15             0 FILE LIFESCI
L16             0 FILE MEDICONF
L17             0 FILE PASCAL

TOTAL FOR ALL FILES
L18             0 EGFRVIII SAME ELISA SAME ANTIBODY

=> 19 same ELISA
MISSING OPERATOR L9 SAME
The search profile that was entered contains terms or
nested terms that are not separated by a logical operator.

=> 19(P)ELISA(P)antibody
L19             0 FILE AGRICOLA
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L2(P)ELISA'
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'ELISA(P)ANTIBODY'
L20             4 FILE BIOTECHNO
L21             0 FILE CONFSCI
L22             0 FILE HEALSAFE
L23             0 FILE IMSDRUGCONF
L24             3 FILE LIFESCI
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L7(P)ELISA'
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'ELISA(P)ANTIBODY'
L25             0 FILE MEDICONF
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L8(P)ELISA'
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'ELISA(P)ANTIBODY'
L26             3 FILE PASCAL

TOTAL FOR ALL FILES
L27            10 L9(P) ELISA(P) ANTIBODY

=> dup rem
ENTER L# LIST OR (END):l27
DUPLICATE IS NOT AVAILABLE IN 'IMSDRUGCONF, MEDICONF'.
ANSWERS FROM THESE FILES WILL BE CONSIDERED UNIQUE
PROCESSING COMPLETED FOR L27
L28             6 DUP REM L27 (4 DUPLICATES REMOVED)

=> d 128 ibib abs total

L28   ANSWER 1 OF 6  BIOTECHNO  COPYRIGHT 2004 Elsevier Science B.V. on STN
      DUPLICATE
ACCESSION NUMBER:         2003:37102750   BIOTECHNO
TITLE:                    Generation of anti-idiotype antibodies for
                          application in clinical immunotherapy laboratory
                          analyses
AUTHOR:                   Liu Z.; Panousis C.; Smyth F.E.; Murphy R.; Wirth V.;
                          Cartwright G.; Johns T.G.; Scott A.M.
CORPORATE SOURCE:         Dr. Z. Liu, Tumour Targeting Laboratory, Ludwig
                          Institute for Cancer Research, Austin/Repatriation
                          Medical Centre, 145-163 Studley Road, Heidelberg, Vic.
                          3084, Australia.
                          E-mail: zhanqi.liu@ludwig.edu.au
```

SOURCE: Hybridoma and Hybridomics, (2003), 22/4 (219-228), 31 reference(s)
CODEN: HHYYBF ISSN: 1536-8599
DOCUMENT TYPE: Journal; Article
COUNTRY: United States
LANGUAGE: English
SUMMARY LANGUAGE: English
AN 2003:37102750 BIOTECHNO
AB The chimeric monoclonal **antibody** ch806 specifically targets the tumor-associated mutant epidermal growth factor receptor (de 2-7EGFR or **EGFRVIII**) and is currently under investigation for its potential use in cancer therapy. The humanised monoclonal **antibody** hu3S193 specifically targets the Lewis Y epithelial antigen and is currently in Phase I clinical trials in patients with advanced breast, colon, and ovarian carcinomas. To assist the clinical evaluation of ch806 and hu3S193, laboratory assays are required to monitor their serum pharmacokinetics and quantitate any immune responses to the **antibodies**. Mice immunized with ch806 or hu3S193 were used to generate hybridomas producing **antibodies** with specific binding to ch806 or hu3S193 and competitive for antigen binding. These anti-idiotype **antibodies** (designated Ludwig Melbourne Hybridomas, LMH) were investigated as reagents suitable for use as positive controls for HAHA or HACA analyses and for measuring hu3S193 or ch806 in human serum. Anti-idiotypes with the ability to concurrently bind two target **antibody** molecules were identified, which enabled the development of highly reproducible, sensitive, specific **ELISA** assays for determining serum concentrations of hu3S193 and ch806 with a 3 ng/mL limit of quantitation using LMH-3 and LMH-12, respectively. BIAcore analyses determined high apparent binding affinity for both idiotypes: LMH-3 binding immobilized hu3S193, Ka = 4.76 x 10.sup.8 M.sup.-.sup.1; LMH-12 binding immobilised ch806, Ka = 1.74 x 10.sup.9 M.sup.-.sup.1. Establishment of HAHA or HACA analysis of sera samples using BIAcore was possible using LMH-3 and LMH-12 as positive controls for quantitation of immune responses to hu3S193 or ch806 in patient sera. These anti-idiotypes could also be used to study the penetrance and binding of ch806 or hu3S193 to tumor cells through immunohistochemical analysis of tumor biopsies. The generation of anti-idiotype **antibodies** capable of concurrently binding a target **antibody** on each variable domain provides reagents with high sensitivity for the assessment of safety and pharmacokinetic profiles of target **antibodies** administered clinically.

L28 ANSWER 2 OF 6 PASCAL COPYRIGHT 2004 INIST-CNRS. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 2002-0194513 PASCAL
COPYRIGHT NOTICE: Copyright .COPYRGT. 2002 INIST-CNRS. All rights reserved.
TITLE (IN ENGLISH): Generation of anti-idiotypic reagents in the **EGFRvIII** tumor-associated antigen system
AUTHOR: WIKSTRAND Carol J.; COLE Vanessa R.; CROTTY Laura E.; SAMPSON John H.; BIGNER Darell D.
CORPORATE SOURCE: Department of Pathology, Box 3156, Medical Center, Duke University Medical Center, Durham, NC 27710, United States; Wake Forest University Baptist Medical Center, Winston-Salem, North Carolina, United States
SOURCE: Cancer immunology and immunotherapy, (2002), 50(12), 639-652, 39 refs.
ISSN: 0340-7004 CODEN: CIIMDN
DOCUMENT TYPE: Journal
BIBLIOGRAPHIC LEVEL: Analytic
COUNTRY: Germany, Federal Republic of
LANGUAGE: English
AVAILABILITY: INIST-16198, 354000102316040010
AN 2002-0194513 PASCAL

AB The use of anti-idiotype (anti-id) vaccines for immunotherapy of human cancers is attractive, as immunization with true anti-id reagents (Ab2β) has been shown to induce both cellular and humoral immunity, frequently when the original antigen does not, or when a state of anergy to the self-expressed tumor-associated antigen exists. The aim of this study was to investigate the potential of an anti-id vaccine approach to the glioma-associated antigen epidermal growth factor receptor variant III (**EGFRvIII**) for human clinical trials. By using conventional methodology, seven rat mAbs specific for the binding site of the murine anti-**EGFRvIII**-specific mAb Y10, as defined by the ability to inhibit the binding of mAb Y10 to **EGFRvIII** expressed on cells or as purified protein, were generated, and a subset (3/7) was found to be true Ab2β, as defined by the ability to induce the formation of **antibody** directed against **EGFRvIII** in two species (mouse and rabbit) when used as immunogen. The ability of these three Ab2β to elicit a protective anti-tumor response when used as a vaccine in the syngeneic, subcutaneous C57B1/ 6-B16mseEGFRvIII tumor model was investigated. Following vaccination with one Ab2β mAb (2C7), 6/20 mice failed to develop tumor upon challenge, and 3/20 mice with outgrowing tumors exhibited dramatic regression of incipient tumors. Vaccination with a second mAb (5G8) resulted in one tumor-free survivor and one tumor regressor; vaccination with the third Ab2β mAb (7D3) did not confer protection, but did significantly increase the latency period until tumor outgrowth in all vaccinated recipients. The ability of Ab2β mAb 2C7 to induce an anti- **EGFRvIII** response in non-human primates was investigated by using the saponin adjuvant approved for human clinical trial, QS-21. Three of three macaques produced anti-**EGFRvIII** titers, as detected on **EGFRvIII** -expressing cells by both **ELISA** and fluorescence-activated cytometric analysis, following six immunizations with Ab2β mAb 2C7 and QS-21. The results obtained confirm that an anti-id response in the **EGFRvIII** antigen system can be induced in rodents, rabbits, and non-human primates, and it may prove a useful adjunct to immunotherapeutic approaches to **EGFRvIII**-positive gliomas, breast carcinomas, and non-small-cell lung tumors.

L28 ANSWER 3 OF 6 LIFESCI COPYRIGHT 2004 CSA on STN
ACCESSION NUMBER: 2003:30690 LIFESCI
TITLE: Generation of anti-idiotypic reagents in the EGFRvIII tumor-associated antigen system
AUTHOR: Wikstrand, C.J.; Cole, V.R.; Crotty, L.E.; Sampson, J.H.; Bigner, D.D.
CORPORATE SOURCE: Department of Pathology, Box 3156, Medical Center, Duke University Medical Center, Durham, NC 27710, USA; E-mail: wikst001@mc.duke.edu
SOURCE: Cancer Immunology, Immunotherapy [Cancer Immunol., Immunother.], (20020200) vol. 50, no. 12, pp. 636-652. ISSN: 0340-7004.
DOCUMENT TYPE: Journal
FILE SEGMENT: F
LANGUAGE: English
SUMMARY LANGUAGE: English
AB The use of anti-idiotype (anti-id) vaccines for immunotherapy of human cancers is attractive, as immunization with true anti-id reagents (Ab2 beta) has been shown to induce both cellular and humoral immunity, frequently when the original antigen does not, or when a state of anergy to the self-expressed tumor-associated antigen exists. The aim of this study was to investigate the potential of an anti-id vaccine approach to the glioma-associated antigen epidermal growth factor receptor variant III (**EGFRvIII**) for human clinical trials. By using conventional methodology, seven rat mAbs specific for the binding site of the murine anti-**EGFRvIII**-specific mAb Y10, as defined by the ability to inhibit the binding of mAb Y10 to **EGFRvIII** expressed on cells or

as purified protein, were generated, and a subset (3/7) was found to be true Ab2 beta , as defined by the ability to induce the formation of **antibody** directed against **EGFRvIII** in two species (mouse and rabbit) when used as immunogen. The ability of these three Ab2 beta to elicit a protective anti-tumor response when used as a vaccine in the syngeneic, subcutaneous C57B1/6-B16mseEGFRvIII tumor model was investigated. Following vaccination with one Ab2 beta mAb (2C7), 6/20 mice failed to develop tumor upon challenge, and 3/20 mice with outgrowing tumors exhibited dramatic regression of incipient tumors. Vaccination with a second mAb (5G8) resulted in one tumor-free survivor and one tumor regressor; vaccination with the third Ab2 beta mAb (7D3) did not confer protection, but did significantly increase the latency period until tumor outgrowth in all vaccinated recipients. The ability of Ab2 beta mAb 2C7 to induce an anti-**EGFRvIII** response in non-human primates was investigated by using the saponin adjuvant approved for human clinical trial, QS-21. Three of three macaques produced anti-**EGFRvIII** titers, as detected on **EGFRvIII**-expressing cells by both **ELISA** and fluorescence-activated cytometric analysis, following six immunizations with Ab2 beta mAb 2C7 and QS-21. The results obtained confirm that an anti-id response in the **EGFRvIII** antigen system can be induced in rodents, rabbits, and non-human primates, and it may prove a useful adjunct to immunotherapeutic approaches to **EGFRvIII** -positive gliomas, breast carcinomas, and non-small-cell lung tumors.

L28 ANSWER 4 OF 6 BIOTECHNO COPYRIGHT 2004 Elsevier Science B.V. on STN
DUPLICATE

ACCESSION NUMBER: 2002:34188683 BIOTECHNO

TITLE: Novel monoclonal **antibody** specific for the de2-7 epidermal growth factor receptor (EGFR) that also recognizes the EGFR expressed in cells containing amplification of the EGFR gene

AUTHOR: Johns T.G.; Stockert E.; Ritter G.; Jungbluth A.A.; Huang H.-J.S.; Cavenee W.K.; Smyth F.E.; Hall C.M.; Watson N.; Nice E.C.; Gullick W.J.; Old L.J.; Burgess A.W.; Scott A.M.

CORPORATE SOURCE: T.G. Johns, Tumour Targeting Program, Ludwig Institute for Cancer Research, Austin Hospital, Studley Rd., Heidelberg, Vic. 3083, Australia.
E-mail: Terry.Johns@ludwig.edu.au

SOURCE: International Journal of Cancer, (20 MAR 2002), 98/3 (398-408), 42 reference(s)
CODEN: IJCNAW ISSN: 0020-7136

DOCUMENT TYPE: Journal; Article

COUNTRY: United States

LANGUAGE: English

SUMMARY LANGUAGE: English

AN 2002:34188683 BIOTECHNO

AB In some respects, the EGFR appears to be an attractive target for tumor-targeted **antibody** therapy: it is overexpressed in many types of epithelial tumor and inhibition of signaling often induces an anti-tumor effect. The use of EGFR specific **antibodies**, however, may be limited by uptake in organs that have high endogenous levels of the wild type EGFR such as the liver. The de2-7 EGFR (or **EGFRvIII**) is a naturally occurring extracellular truncation of the EGFR found in a number of tumor types including glioma, breast, lung and prostate. **Antibodies** directed to this tumor specific variant of the EGFR provide an alternative targeting strategy, although the lower proportion of tumors that express the de2-7 EGFR restricts this approach. We describe a novel monoclonal **antibody** (MAb 806) that potentially overcomes the difficulties associated with targeting the EGFR expressed on the surface of tumor cells. MAb 806 bound to de2-7 EGFR transfected U87MG glioma cells (U87MG.Δ2-7) with high affinity (.apprx.1 x 10.sup.9 M.sup.-.sup.1), but did not bind parental cells that express the wild type EGFR. Consistent with this observation, MAb

806 was unable to bind a soluble version of the wild type EGFR containing the extracellular domain. In contrast, immobilization of this extracellular domain to **ELISA** plates induced saturating and dose response binding of MAb 806, suggesting that MAb 806 can bind the wild type EGFR under certain conditions. MAb 806 also bound to the surface of A431 cells, which due to an amplification of the EGFR gene express large amounts of the EGFR. Interestingly, MAb 806 only recognized 10% of the total EGFR molecules expressed by A431 cells and the binding affinity was lower than that determined for the de2-7 EGFR. MAb 806 specifically targeted U87MG.Δ2-7 and A431 xenografts grown in nude mice with peak levels in U87MG.Δ2-7 xenografts detected 8 h after injection. No specific targeting of parental U87MG xenografts was observed. Following binding to U87MG.Δ2-7 cells, MAb 806 was rapidly internalized by macropinocytosis and subsequently transported to lysosomes, a process that probably contributes to the early targeting peak observed in the xenografts. Thus, MAb 806 can be used to target tumor cells containing amplification of the EGFR gene or de2-7 EGFR but does not bind to the wild type EGFR when expressed on the cell surface. .COPYRGT. 2002 Wiley-Liss, Inc.

L28 ANSWER 5 OF 6 BIOTECHNO COPYRIGHT 2004 Elsevier Science B.V. on STN
ACCESSION NUMBER: 2001:34146569 BIOTECHNO
TITLE: Generation of anti-idiotypic reagents in the **EGFRvIII** tumor-associated antigen system
AUTHOR: Wikstrand C.J.; Cole V.R.; Crotty L.E.; Sampson J.H.; Bigner D.D.
CORPORATE SOURCE: C.J. Wikstrand, Department of Pathology, Box 3156, Duke University Medical Center, Durham, NC 27710, United States.
E-mail: wikst001@mc.duke.edu
SOURCE: Cancer Immunology, Immunotherapy, (2001), 50/12 (639-652), 39 reference(s)
CODEN: CIIMDN ISSN: 0340-7004
DOCUMENT TYPE: Journal; Article
COUNTRY: Germany, Federal Republic of
LANGUAGE: English
SUMMARY LANGUAGE: English
AN 2001:34146569 BIOTECHNO
AB The use of anti-idiotype (anti-id) vaccines for immunotherapy of human cancers is attractive, as immunization with true anti-id reagents (Ab2β) has been shown to induce both cellular and humoral immunity, frequently when the original antigen does not, or when a state of anergy to the self-expressed tumor-associated antigen exists. The aim of this study was to investigate the potential of an anti-id vaccine approach to the glioma-associated antigen epidermal growth factor receptor variant III (**EGFRvIII**) for human clinical trials. By using conventional methodology, seven rat mAbs specific for the binding site of the murine anti-**EGFRvIII**-specific mAb Y10, as defined by the ability to inhibit the binding of mAb Y10 to **EGFRvIII** expressed on cells or as purified protein, were generated, and a subset (3/7) was found to be true Ab2β, as defined by the ability to induce the formation of **antibody** directed against **EGFRvIII** in two species (mouse and rabbit) when used as immunogen. The ability of these three Ab2β to elicit a protective anti-tumor response when used as a vaccine in the syngeneic, subcutaneous C57Bl/6-B16mseEGFRvIII tumor model was investigated. Following vaccination with one Ab2β mAb (2C7), 6/20 mice failed to develop tumor upon challenge, and 3/20 mice with outgrowing tumors exhibited dramatic regression of incipient tumors. Vaccination with a second mAb (5G8) resulted in one tumor-free survivor and one tumor regressor; vaccination with the third Ab2β mAb (7D3) did not confer protection, but did significantly increase the latency period until tumor outgrowth in all vaccinated recipients. The ability of Ab2β mAb 2C7 to induce an anti- **EGFRvIII** response in non-human primates was investigated by using the saponin adjuvant

approved for human clinical trial, QS-21. Three of three macaques produced anti-**EGFRvIII** titers, as detected on **EGFRvIII** -expressing cells by both **ELISA** and fluorescence-activated cytometric analysis, following six immunizations with Ab2β mAb 2C7 and QS-21. The results obtained confirm that an anti-id response in the **EGFRvIII** antigen system can be induced in rodents, rabbits, and non-human primates, and it may prove a useful adjunct to immunotherapeutic approaches to **EGFRvIII**-positive gliomas, breast carcinomas, and non-small-cell lung tumors.

L28 ANSWER 6 OF 6 BIOTECHNO COPYRIGHT 2004 Elsevier Science B.V. on STN
DUPLICATE

ACCESSION NUMBER: 1995:25216942 BIOTECHNO
TITLE: Monoclonal **antibodies** against **EGFRvIII** are tumor specific and react with breast and lung carcinomas and malignant gliomas
AUTHOR: Wikstrand C.J.; Hale L.P.; Batra S.K.; Hill M.L.; Humphrey P.A.; Kurpad S.N.; McLendon R.E.; Moscatello D.; Pegram C.N.; Reist C.J.; Traweek S.T.; Wong A.J.; Zalutsky M.R.; Bigner D.D.
CORPORATE SOURCE: Pathology Department, Duke University Medical Center, Box 3156,Durham, NC 27710, United States.
SOURCE: Cancer Research, (1995), 55/14 (3140-3148)
CODEN: CNREA8 ISSN: 0008-5472
DOCUMENT TYPE: Journal; Article
COUNTRY: United States
LANGUAGE: English
SUMMARY LANGUAGE: English
AN 1995:25216942 BIOTECHNO
AB Despite molecular biological advances in understanding human cancers, translation into therapy has been less forthcoming; targeting neoplastic cells still requires that tumor-specific markers, preferably those on the cell surface, be identified. The epidermal growth factor receptor (EGFR) exists in a deletion-mutant form, **EGFRvIII**, which has been identified by genetic and immunological means in a subset of gliomas and non-small cell lung carcinomas. Specific polyvalent antisera to the extracellular portion of the variant were readily induced, but immunization using a synthetic linear peptide representing the unique **EGFRvIII** primary sequence has been unsuccessful in mice or macaques. We report here five specific monoclonal **antibodies** (mAbs) developed through long-term immunization protocols using the **EGFRvIII**-specific synthetic peptide and the intact variant in different formats that maintained secondary and tertiary conformation. These mAbs identify the **EGFRvIII** on the cell surface with relatively high affinity (K(A) range, 0.13 to 2.5 x 10.sup.9 M.sup.-.sup.1) by live cell Scatchard analysis. These mAbs are specific fur **EGFRvIII** as determined by RIA, **ELISA**, Western blot, analytical flow cytometry, autophosphorylation, and immunohistochemistry. Isolating specific mAbs enabled us tn analyze normal and neoplastic human tissue and establish that **EGFRvIII** is truly tumor specific for subsets of breast carcinomas and for previously reported non-small cell lung carcinomas and gliomas. Also, this receptor is not expressed by any normal human tissues thus far examined, including elements of the peripheral, central nervous, and lymphoid systems. With mAbs, we identified a higher incidence of **EGFRvIII** positivity in gliomas than previously described and identified an **EGFRvIII**- positive subset of breast tumors; also, we observed that the **EGFRvIII** epitope is not expressed in normal tissues, and we demonstrated the localizing and therapeutic potential of the mAbs for tumors expressing this epitope. Our observations strongly warrant development of this mAb-antigen system as therapy for breast, lung, and central nervous system tumors.

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=> file .chemistry
COST IN U.S. DOLLARS                                    SINCE FILE      TOTAL
                                                           ENTRY    SESSION
FULL ESTIMATED COST                                        29.46      29.67

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FILE 'USPATFULL' ENTERED AT 10:43:15 ON 15 JUN 2004
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=> EGFRvIII(P)ELISA(P)antibody
L29             5 FILE CAPLUS
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'EGFRVIII(P)ELISA'
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'ELISA(P)ANTIBODY'
L30             4 FILE BIOTECHNO
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'EGFRVIII(P)ELISA'
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'ELISA(P)ANTIBODY'
L31             0 FILE COMPENDEX
L32             0 FILE ANABSTR
L33             0 FILE CERAB
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'EGFRVIII(P)ELISA'
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'ELISA(P)ANTIBODY'
L34             0 FILE METADEX
L35             2 FILE USPATFULL

TOTAL FOR ALL FILES
L36            11 EGFRVIII(P) ELISA(P) ANTIBODY

=> dup rem
ENTER L# LIST OR (END):l36
PROCESSING COMPLETED FOR L36
L37             8 DUP REM L36 (3 DUPLICATES REMOVED)

=> d l37 ibib abs total

L37  ANSWER 1 OF 8  USPATFULL on STN
ACCESSION NUMBER:       2003:299876  USPATFULL
TITLE:                  Anti-egfrvIII scfvs with improved cytotoxicity and
```

yield, immunotoxins based thereon, and methods of use thereof

INVENTOR(S): Pastan, Ira, Potomac, MD, UNITED STATES
Beers, Richard, Washington, DC, UNITED STATES
Chowdhury, Partha S, Rockville, MD, UNITED STATES
Bigner, Darell, Mebane, NC, UNITED STATES

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 2003211097	A1	20031113	
APPLICATION INFO.:	US 2002-203675	A1	20020809	(10)
	WO 2001-US5923		20010223	

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: TOWNSEND AND TOWNSEND AND CREW, LLP, TWO EMBARCADERO CENTER, EIGHTH FLOOR, SAN FRANCISCO, CA, 94111-3834
NUMBER OF CLAIMS: 45
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 6 Drawing Page(s)
LINE COUNT: 2584
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The invention provides antibodies for a mutant form of the epidermal growth factor receptor known as EGFRvIII. This mutant is found only or primarily on the surface of glioblastoma cells, and on cells of breast, ovarian and non-small cell lung carcinomas. The antibodies provided by the invention have higher affinity for EGFRvIII, and form immunotoxins with higher cytotoxicity and yield, than prior art antibodies, including the scFv designated MR1. In particular, the invention provides an antibody, designated MR1-1, which mutates MR1 in the CDR3 of the VH and VL chains to provide an antibody with especially good cytotoxicity. The invention provides additional antibodies in which MR1 is mutated in the CDR1 and 2 of VH or VL, or both, with better binding to EGFRvIII than that of the parental MR1 antibody.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L37 ANSWER 2 OF 8 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 1
ACCESSION NUMBER: 2003:722393 CAPLUS
DOCUMENT NUMBER: 139:363168
TITLE: Generation of Anti-Idiotype Antibodies for Application in Clinical Immunotherapy Laboratory Analyses
AUTHOR(S): Liu, Zhanqi; Panousis, Con; Smyth, Fiona E.; Murphy, Roger; Wirth, Veronika; Cartwright, Glenn; Johns, Terrance G.; Scott, Andrew M.
CORPORATE SOURCE: Melbourne Tumor Biology Branch, Austin & Repatriation Medical Centre, Institute for Cancer Research, Heidelberg, Australia
SOURCE: Hybridoma and Hybridomics (2003), 22(4), 219-228
CODEN: HHYYBF; ISSN: 1536-8599
PUBLISHER: Mary Ann Liebert, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The chimeric monoclonal **antibody** ch806 specifically targets the tumor-associated mutant epidermal growth factor receptor (de 2-7EGFR or **EGFRVIII**) and is currently under investigation for its potential use in cancer therapy. The humanized monoclonal **antibody** hu3S193 specifically targets the Lewis Y epithelial antigen and is currently in Phase I clin. trials in patients with advanced breast, colon, and ovarian carcinomas. To assist the clin. evaluation of ch806 and hu3S193, laboratory assays are required to monitor their serum pharmacokinetics and quantitate any immune responses to the **antibodies**. Mice immunized with ch806 or hu3S193 were used to generate hybridomas producing **antibodies** with specific binding to ch806 or hu3S193 and competitive for antigen binding. These anti-idiotype **antibodies**

(designated Ludwig Melbourne Hybridomas, LMH) were investigated as reagents suitable for use as pos. controls for HAHA or HACA analyses and for measuring hu3S193 or ch806 in human serum. Anti-idiotypes with the ability to concurrently bind two target **antibody** mols. were identified, which enabled the development of highly reproducible, sensitive, specific **ELISA** assays for determining serum concns. of hu3S193 and ch806 with a 3 ng/mL limit of quantitation using LMH-3 and LMH-12, resp. BIAcore analyses determined high apparent binding affinity for both idiotypes: LMH-3 binding immobilized hu3S193, Ka = 4.76+108 M-1; LMH-12 binding immobilized ch806, Ka = 1.74+109 M-1. Establishment of HAHA or HACA anal. of sera samples using BIAcore was possible using LMH-3 and LMH-12 as pos. controls for quantitation of immune responses to hu3S193 or ch806 in patient sera. These anti-idiotypes could also be used to study the penetrance and binding of ch806 or hu3S193 to tumor cells through immunohistochem. anal. of tumor biopsies. The generation of anti-idiotype **antibodies** capable of concurrently binding a target **antibody** on each variable domain provides reagents with high sensitivity for the assessment of safety and pharmacokinetic profiles of target **antibodies** administered clin.

REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L37 ANSWER 3 OF 8 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:274800 CAPLUS
DOCUMENT NUMBER: 137:139020
TITLE: Generation of anti-idiotypic reagents in the EGFRvIII tumor-associated antigen system
AUTHOR(S): Wikstrand, Carol J.; Cole, Vanessa R.; Crotty, Laura E.; Sampson, John H.; Bigner, Darell D.
CORPORATE SOURCE: Department of Pathology, Duke University Medical Center, Durham, NC, 27710, USA
SOURCE: Cancer Immunology Immunotherapy (2002), 50(12), 639-652
CODEN: CIIMDN; ISSN: 0340-7004
PUBLISHER: Springer-Verlag
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The use of anti-idiotype (anti-id) vaccines for immunotherapy of human cancers is attractive, as immunization with true anti-id reagents (Ab2β) has been shown to induce both cellular and humoral immunity, frequently when the original antigen does not, or when a state of anergy to the self-expressed tumor-associated antigen exists. The aim of this study was to investigate the potential of an anti-id vaccine approach to the glioma-associated antigen epidermal growth factor receptor variant III (**EGFRvIII**) for human clin. trials. By using conventional methodol., seven rat mAbs specific for the binding site of the murine anti-**EGFRvIII**-specific mAb Y10, as defined by the ability to inhibit the binding of mAb Y10 to **EGFRvIII** expressed on cells or as purified protein, were generated, and a subset (3/7) was found to be true Ab2β, as defined by the ability to induce the formation of **antibody** directed against **EGFRvIII** in two species (mouse and rabbit) when used as immunogen. The ability of these three Ab2β to elicit a protective anti-tumor response when used as a vaccine in the syngeneic, s.c. C57Bl/6-B16mseEGFRvIII tumor model was investigated. Following vaccination with one Ab2β mAb (2C7), 6/20 mice failed to develop tumor upon challenge, and 3/20 mice with outgrowing tumors exhibited dramatic regression of incipient tumors. Vaccination with a second mAb (5G8) resulted in one tumor-free survivor and one tumor regressor; vaccination with the third Ab2β mAb (7D3) did not confer protection, but did significantly increase the latency period until tumor outgrowth in all vaccinated recipients. The ability of Ab2β mAb 2C7 to induce an anti-**EGFRvIII** response in non-human primates was investigated by using the saponin adjuvant approved for human clin. trial, QS-21. Three of three macaques produced anti-**EGFRvIII** titers,

as detected on **EGFRvIII**-expressing cells by both **ELISA** and fluorescence-activated cytometric anal., following six immunizations with Ab2β mAb 2C7 and QS-21. The results obtained confirm that an anti-id response in the **EGFRvIII** antigen system can be induced in rodents, rabbits, and non-human primates, and it may prove a useful adjunct to immunotherapeutic approaches to **EGFRvIII**-pos. gliomas, breast carcinomas, and non-small-cell lung tumors.

REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L37 ANSWER 4 OF 8 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 2

ACCESSION NUMBER: 2002:201095 CAPLUS

DOCUMENT NUMBER: 136:323694

TITLE: Novel monoclonal antibody specific for the DE2-7 epidermal growth factor receptor (EGFR) that also recognizes the EGFR expressed in cells containing amplification of the EGFR gene

AUTHOR(S): Johns, Terrance G.; Stockert, Elisabeth; Ritter, Gerd; Jungbluth, Achim A.; Huang, H.-J. Su; Cavenee, Webster K.; Smyth, Fiona E.; Hall, Cathrine M.; Watson, Nadine; Nice, Edouard C.; Gullick, William J.; Old, Lloyd J.; Burgess, Antony W.; Scott, Andrew M.

CORPORATE SOURCE: Tumour Targeting Program, Ludwig Institute for Cancer Research, Melbourne, Australia

SOURCE: International Journal of Cancer (2002), 98(3), 398-408
CODEN: IJCNAW; ISSN: 0020-7136

PUBLISHER: Wiley-Liss, Inc.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB In some respects, the EGFR appears to be an attractive target for tumor-targeted **antibody** therapy: it is overexpressed in many types of epithelial tumor and inhibition of signaling often induces an anti-tumor effect. The use of EGFR specific **antibodies**, however, may be limited by uptake in organs that have high endogenous levels of the wild type EGFR such as the liver. The de2-7 EGFR (or **EGFRvIII**) is a naturally occurring extracellular truncation of the EGFR found in a number of tumor types including glioma, breast, lung and prostate. **Antibodies** directed to this tumor specific variant of the EGFR provide an alternative targeting strategy, although the lower proportion of tumors that express the de2-7 EGFR restricts this approach. The authors describe a novel monoclonal **antibody** (MAb 806) that potentially overcomes the difficulties associated with targeting the EGFR expressed on the surface of tumor cells. MAb 806 bound to de2-7 EGFR transfected U87MG glioma cells (U87MG.Δ2-7) with high affinity (.apprx.1+109 M-1), but did not bind parental cells that express the wild type EGFR. Consistent with this observation, MAb 806 was unable to bind a soluble version of the wild type EGFR containing the extracellular domain.

In contrast, immobilization of this extracellular domain to **ELISA** plates induced saturating and dose response binding of MAb 806, suggesting that MAb 806 can bind the wild type EGFR under certain conditions. MAb 806 also bound to the surface of A431 cells, which due to an amplification of the EGFR gene express large amts. of the EGFR. Interestingly, MAb 806 only recognized 10% of the total EGFR mols. expressed by A431 cells and the binding affinity was lower than that determined for the de2-7 EGFR. MAb 806 specifically targeted U87MG.Δ2-7 and A431 xenografts grown in nude mice with peak levels in U87MG.Δ2-7 xenografts detected 8 h after injection. No specific targeting of parental U87MG xenografts was observed Following binding to U87MG.Δ2-7 cells, MAb 806 was rapidly internalized by macropinocytosis and subsequently transported to lysosomes, a process that probably contributes to the early targeting peak observed in the xenografts. Thus, MAb 806 can be used to target tumor cells containing amplification of the EGFR gene or de2-7 EGFR but does not bind to the wild type EGFR when expressed on the cell surface.

REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L37 ANSWER 5 OF 8 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:693382 CAPLUS
DOCUMENT NUMBER: 135:256132
TITLE: Sensitive detection of wild-type and mutant EGFR by specific ELISA assays in any biological sample
INVENTOR(S): Wong, Albert J.; Leitzel, Kim E.; Moscatello, David K.; Lipton, Allan
PATENT ASSIGNEE(S): Thomas Jefferson University, USA
SOURCE: PCT Int. Appl., 22 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001068711	A1	20010920	WO 2001-US7766	20010312
W: CA, JP				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR				
US 2001046686	A1	20011129	US 2001-803854	20010312
EP 1276771	A1	20030122	EP 2001-918548	20010312
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY, TR				

PRIORITY APPLN. INFO.: US 2000-188424P P 20000310
WO 2001-US7766 W 20010312

AB The present invention generally relates to a method of detecting type III mutant EGF receptor (EGFRvIII) in biol. samples, a method of detecting cancers and other diseases in biol. samples, and to a method of assessing treatment and selecting therapy for cancer patients.

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L37 ANSWER 6 OF 8 USPATFULL on STN
ACCESSION NUMBER: 2001:218198 USPATFULL
TITLE: Sensitive detection of wild-type and mutant EGFR by specific ELISA assays in any biological sample
INVENTOR(S): Wong, Albert J., Philadelphia, PA, United States
Leitzel, Kim E., Hummelstown, PA, United States
Moscatello, David K., Philadelphia, PA, United States
Lipton, Allan, Hershey, PA, United States

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 2001046686	A1	20011129	
APPLICATION INFO.:	US 2001-803854	A1	20010312	(9)

	NUMBER	DATE	
PRIORITY INFORMATION:	US 2000-188424P	20000310	(60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: THOMAS JEFFERSON UNIVERSITY, INTELLECTUAL PROPERTY DIVISION, 1020 WALNUT STREET, SUITE 620, PHILADELPHIA, PA, 19107
NUMBER OF CLAIMS: 20
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 1 Drawing Page(s)
LINE COUNT: 475
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention generally relates a method of detecting type III mutant EGF receptor (EGFRvIII) in biological samples, a method of detecting cancers and other diseases in biological samples, and to a method of assessing treatment and selecting therapy for cancer patients.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L37 ANSWER 7 OF 8 BIOTECHNO COPYRIGHT 2004 Elsevier Science B.V. on STN
ACCESSION NUMBER: 2001:34146569 BIOTECHNO
TITLE: Generation of anti-idiotypic reagents in the **EGFRvIII** tumor-associated antigen system
AUTHOR: Wikstrand C.J.; Cole V.R.; Crotty L.E.; Sampson J.H.; Bigner D.D.
CORPORATE SOURCE: C.J. Wikstrand, Department of Pathology, Box 3156, Duke University Medical Center, Durham, NC 27710, United States.
E-mail: wikst001@mc.duke.edu
SOURCE: Cancer Immunology, Immunotherapy, (2001), 50/12 (639-652), 39 reference(s)
CODEN: CIIMDN ISSN: 0340-7004
DOCUMENT TYPE: Journal; Article
COUNTRY: Germany, Federal Republic of
LANGUAGE: English
SUMMARY LANGUAGE: English
AN 2001:34146569 BIOTECHNO
AB The use of anti-idiotype (anti-id) vaccines for immunotherapy of human cancers is attractive, as immunization with true anti-id reagents (Ab2β) has been shown to induce both cellular and humoral immunity, frequently when the original antigen does not, or when a state of anergy to the self-expressed tumor-associated antigen exists. The aim of this study was to investigate the potential of an anti-id vaccine approach to the glioma-associated antigen epidermal growth factor receptor variant III (**EGFRvIII**) for human clinical trials. By using conventional methodology, seven rat mAbs specific for the binding site of the murine anti-**EGFRvIII**-specific mAb Y10, as defined by the ability to inhibit the binding of mAb Y10 to **EGFRvIII** expressed on cells or as purified protein, were generated, and a subset (3/7) was found to be true Ab2β, as defined by the ability to induce the formation of **antibody** directed against **EGFRvIII** in two species (mouse and rabbit) when used as immunogen. The ability of these three Ab2β to elicit a protective anti-tumor response when used as a vaccine in the syngeneic, subcutaneous C57Bl/6-B16mseEGFRvIII tumor model was investigated. Following vaccination with one Ab2β mAb (2C7), 6/20 mice failed to develop tumor upon challenge, and 3/20 mice with outgrowing tumors exhibited dramatic regression of incipient tumors. Vaccination with a second mAb (5G8) resulted in one tumor-free survivor and one tumor regressor; vaccination with the third Ab2β mAb (7D3) did not confer protection, but did significantly increase the latency period until tumor outgrowth in all vaccinated recipients. The ability of Ab2β mAb 2C7 to induce an anti- **EGFRvIII** response in non-human primates was investigated by using the saponin adjuvant approved for human clinical trial, QS-21. Three of three macaques produced anti-**EGFRvIII** titers, as detected on **EGFRvIII** -expressing cells by both **ELISA** and fluorescence-activated cytometric analysis, following six immunizations with Ab2β mAb 2C7 and QS-21. The results obtained confirm that an anti-id response in the **EGFRvIII** antigen system can be induced in rodents, rabbits, and non-human primates, and it may prove a useful adjunct to immunotherapeutic approaches to **EGFRvIII**-positive gliomas, breast carcinomas, and non-small-cell lung tumors.

L37 ANSWER 8 OF 8 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 3
ACCESSION NUMBER: 1995:688164 CAPLUS
DOCUMENT NUMBER: 123:109747

TITLE: Monoclonal antibodies against EGFRvIII are tumor specific and react with breast and lung carcinomas and malignant gliomas

AUTHOR(S): Wikstrand, Carol J.; Hale, Laura P.; Batra, Surinder K.; Hill, M. Leslie; Humphrey, Peter A.; Kurpad, Shekar N.; McLendon, Roger E.; Moscatello, David; Pegram, Charles N.; et al.

CORPORATE SOURCE: Dep. of Pathology and Radiology, Barnes Hospital, St. Louis, MO, 63110, USA

SOURCE: Cancer Research (1995), 55(14), 3140-8
CODEN: CNREA8; ISSN: 0008-5472

PUBLISHER: American Association for Cancer Research

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Despite mol. biol. advances in understanding human cancers, translation into therapy has been less forthcoming; targeting neoplastic cells still requires that tumor-specific markers, preferably those on the cell surface, be identified. The epidermal growth factor receptor (EGFR) exists in a deletion-mutant form, **EGFRvIII**, which has been identified by genetic and immunol. means in a subset of gliomas and non-small cell lung carcinomas. Specific polyvalent antisera to the extra-cellular portion of the variant were readily induced, but immunization using a synthetic linear peptide representing the unique **EGFRvIII** primary sequence has been unsuccessful in mice or macaques. We report here five specific monoclonal **antibodies** (mAbs) developed through long-term immunization protocols using the **EGFRvIII**-specific synthetic peptide and the intact variant in different formats that maintained secondary and tertiary conformation. These mAbs identify the **EGFRvIII** on the cell surface with relatively high affinity (KA range, 0.13 to 2.5 + 109 M-1) by live cell Scatchard anal. These mAbs are specific for **EGFRvIII** as determined by RIA, **ELISA**, Western blot, anal. flow cytometry, autophosphorylation, and immunohistochem. Isolating specific mAbs enabled us to analyze normal and neoplastic human tissue and establish the **EGFRvIII** as truly tumor specific for subsets of breast carcinomas and for previously reported non-small cell lung carcinomas and gliomas. Also, this receptor is not expressed by any normal human tissues thus far examined, including elements of the peripheral, central nervous, and lymphoid systems. With mAbs, we identified a higher incidence of EGFR-vIII positivity in gliomas than previously described and identified an **EGFRvIII**-pos. subset of breast tumors; also, we observed that the **EGFRvIII** epitope is not expressed in normal tissues, and we demonstrated the localizing and therapeutic potential of the mAbs for tumors expressing this epitope. Our observations strongly warrant development of this mAb-antigen system as therapy for breast, lung, and central nervous system tumors.

EGFRvIII(P)(serum, urine, CSF, amniotic, lung sputum, or extracts)